

REMARKS

Claims 1-11 and 14-23 are pending in the present application. Claims 14-17 have been withdrawn from consideration by the Office. Claims 1, 2, 8, 19, and 20 have been amended herein, support for which can be found throughout the specification and in the examples. Upon entry of the present amendment, claims 1-11 and 14-23 will remain pending in this application.

Applicants note, with appreciation, that the Office did not repeat the rejection under 35 U.S.C. §112, second paragraph in the present Office Action. Accordingly, Applicants presume that this rejection has been withdrawn.

I. Nonstatutory Obviousness-Type Double Patenting Rejection

Claims 1-2 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-4 and 8 of co-pending U.S. Patent Publ. No. 2007/0099957 (hereinafter “the ‘957 publication”), and claim 11 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claim 5 of the ‘957 publication. Claims 1, 2, and 11 are also rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-4 and 8 of U.S. Patent Appl. No. 10/555,980 (hereinafter “the ‘980 application”). As a preliminary matter, Applicants respectfully note that the ‘980 application and the ‘957 publication are, indeed, the same application. For the sake of clarity, Applicants refer to the ‘957 publication throughout this section of the response. In addition, claims 1, 6, 7, 8, 10, and 14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1, 4, 8, 15, 16, and 18 of co-pending U.S. Patent Appl. No. 10/596,850 (hereinafter “the ‘850 application”).

Applicants respectfully submit that the present application is a §371 application of PCT Appl. No. PCT/SE2003/001705 filed November 5, 2003, whereas the ‘957 publication is a §371 application of PCT Appl. No. PCT/GB2004/002074 filed May 13, 2004, and the ‘850 application is a §371 application of PCT Appl. No. PCT/GB2004/002074 filed May 13, 2004. As such, the present application is the earlier filed of the applications. Applicants respectfully assert that when a “provisional” nonstatutory obviousness-type double patenting rejection is the only rejection remaining in the earlier filed of two pending applications, the Office should withdraw the

obviousness-type double patenting rejection in the earlier filed case and permit it to issue without requiring a terminal disclaimer. As a result, Applicants will await a notice of allowable subject matter in the application at issue before responding further.

The Office stated that this rejection is “maintained because [it is] not the only outstanding issue in this application” (see, Office Action at page 12). Applicants respectfully point out that they are not requesting the Office to withdraw this rejection but, rather, only request the Office to hold this rejection in abeyance until the claims are otherwise allowable. It is premature for Applicants to address this rejection substantively at the present time.

II. The Claimed Invention Is Not Obvious

Claims 1-10 are rejected under 35 U.S.C. §103(a) as allegedly being obvious over PCT Publication No. WO98/28275 (hereinafter “Delorme”). Applicants traverse the rejection and respectfully request reconsideration of the same.

Delorme does not teach or suggest the presently claimed invention. The presently claimed invention comprises a **substituted** amino group at the *meta* position of the phenyl ring i.e., R¹ is not hydrogen. In contrast, the Example 41 compound of Delorme has an **unsubstituted** amino group on the phenyl ring at issue(see, page 69 of the Delorme reference). A reference teaches away from a claimed invention when the reference does not suggest that a person of ordinary skill experiment in the claimed direction. A reference must be considered as a whole requiring the Office to consider the portions of the reference that teach away from the claimed invention. Thus, a teaching away from the art is a per se demonstration of lack of a *prima facie* case of obviousness. *In re Dow Chemical Co.*, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988); *In re Fine*, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988); and *In re Nielson*, 2 U.S.P.Q.2d 1525 (Fed. Cir. 1987). Further, Delorme discloses a large genus comprising a large number of values for moieties A, B, R¹, R², and R³. One of ordinary skill in the art would not have been motivated to choose Applicants’ particular substituted phenyl ring from the multitude of variables reported for the A and B rings of Delorme, let alone suggest combining the substituted phenyl ring of the presently claimed invention with the R¹, R² and R³ groups of the presently claimed invention. Indeed, Delorme does not provide any suggestion that would have motivated one of ordinary

skill in the art to replace one of the Delorme Example 41 amino group hydrogens, let alone suggest combining even one of presently claimed R¹ groups therewith. Further, the Federal Circuit has made it clear that a claimed compound is not obvious over a prior art compound unless there is “a preliminary finding that one of ordinary skill in the art would have selected [the prior art compound]...as a lead compound.” *Takeda Chemical Industries, Ltd. v. Alphapharm Pty, Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. 2007) (finding a claimed compound non-obvious because one of ordinary skill in the art would not have selected the prior art compound as the lead compound out of the “hundreds of millions” of compounds disclosed by the prior art patent). As the Delorme reference fails to provide any motivation that would have led one of ordinary skill in the art to choose the compound of Example 41 as a lead compound out of the many compounds covered by the generic formula therein, Applicants respectfully assert that claims 1-10 are not obvious over the Delorme reference. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §103(a) be withdrawn.

III. The Claimed Invention is Enabled

Claims 1-10 and 18-23 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. Applicants thank the Office for identifying the portions of the claimed invention considered enabled. (see, Office Action at pages 5-6).

The Office, however, alleges the specification “does not reasonably provide enablement for using the compounds of Formula I where R1, R2, and R3 equal to any of the other moieties claimed” (see, Office Action at page 6). Applicants traverse the rejection and respectfully request reconsideration thereof because undue experimentation is not required to practice “the other moieties” at issue.

As will be recognized, the enablement requirement of §112 is satisfied as long as a disclosure contains a sufficient amount of information that persons of ordinary skill in the art having the disclosure before them are able to make and use the invention. *In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988) (the legal standard for enablement under §112 is whether one skilled in the art would be able to practice the invention without undue experimentation). In this respect, the following statement from *In re Marzocchi*, is noteworthy:

As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented **must** be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. Assuming that sufficient reason for such doubt does exist, a rejection for failure to teach how to make and/or use will be proper on that basis; such a rejection can be overcome by suitable proofs indicating that the teaching contained in the specification is truly enabling.

... it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.

169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971). Thus, any assertion by the Office that an enabling disclosure is not commensurate in scope with the protection sought must be supported by evidence or reasoning substantiating the doubts so expressed. *In re Dinh-Nguyen*, 181 U.S.P.Q. 46 (C.C.P.A. 1974); *In re Bowen*, 181 U.S.P.Q. 48 (C.C.P.A. 1974).

The Office asserts the following regarding determining the activity of compounds other than those admittedly enabled (see above): “Considering the large number of compounds to be made this is a large quantity of experimentation.” The Office further asserts that “determining [if any species not particularly disclosed as examples] would be active would require synthesis of the substrate and subjecting it to testing [in] Applicants’ GTP binding assay” and that “[t]he direction [provided] in pages 39 -75 [sic] . . . merely states Applicant’s intent to make and use such compounds” (See, Office Action at page 6).

The case law, however is quite clear that even voluminous research is not undue so long as it is of a routine nature. *Ex parte Forman*, 230 U.S.P.Q. 546, 547 (Pat. Off. Bd. App. 1986). “The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.” *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing *In re Angstadt*,

537 F.2d 489, 502-04, 190 USPQ 214, 217-19 (CCPA 1976)).

In accordance with *Wands*, Applicants' specification provides ample guidance with respect to the direction in which the experimentation should proceed (see, for example, pages 28-36 of the specification). Indeed, Applicants' specification does more than evidence an "intent" to make compounds, it discloses 12 synthesis schemes and 54 examples teaching how to make compounds in accordance with the claimed invention. (see, pages 22-28 and 36-77 of the specification). Moreover, persons of ordinary skill in the art routinely test compounds in binding assays, such as, for example the GTP binding assay described at pages 30-31 of the application at issue. As any experimentation needed under the circumstance at issue—even if a large amount of experimentation—would be routine and the specification at issue provides a reasonable amount of guidance, Applicants respectfully assert the "compounds of Formula I where R1, R2, and R3 equal to any of the other moieties claimed" are enabled.

The Office also asserts "none of the working examples contains any radical R1-R3 equal to any of the moieties claimed other than the ones enabled above" (see, Office Action at page 6), and Applicants' specification does not enable the entire scope of the claims. (see, Office Action at pages 7-9).

Applicants remind the Examiner that a working example is not mandatory if none actually exists and the invention is otherwise disclosed so that one skilled in the art can practice it without undue experimentation. *In re Borkowski et al.*, 164 USPQ 642 (Fed. Cir. 1970); *In re Gay*, 135 U.S.P.Q. 311 (C.C.P.A. 1962); *In re Stephens*, 188 U.S.P.Q. 659 (C.C.P.A. 1976); and *Ex parte Krenzer*, 199 U.S.P.Q. 227 (Pat. Off. Bd. App. 1978). See also, *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 224 U.S.P.Q. 409 (Fed. Cir. 1984) (holding use of "prophetic" examples or intended examples does not automatically make a patent non-enabling merely because there can be no guarantee that the examples will actually work). Moreover, Applicants "are not required to disclose every species encompassed by their claims even in an unpredictable art" for a generic claim to be fully enabled. See, *In re Angstadt*, 537 F.2d 498, 502 (C.C.P.A. 1976) (finding a generic claim enabled where the specification disclosed 40 examples).

In this regard, Applicants have provided Examples of compounds having one or more moieties for each of the “R” groups recited in amended claim 1. The following table shows the support in Applicants’ specification.

| Variable | Compound No(s). |
|---|--|
| R¹ | |
| C ₃₋₆ alkyl | 12 |
| C ₆₋₁₀ aryl | 35, 36, 37 |
| C ₆₋₁₀ aryl-C ₁₋₄ alkyl | 1, 4, 5, 6, 7, 8, 38, 39, 42 |
| C ₂₋₉ heteroaryl-C ₁₋₄ alkyl | 2, 3, 9, 10 |
| C ₃₋₁₀ cycloalkyl | 13, 14, 15, 16, 43 |
| C ₃₋₁₀ cycloalkyl-C ₁₋₄ alkyl | 11, 40, 41 |
| R ⁸ -C(=O)- | 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 46, 47, 48, 49, 50, 51, 52, 53 |
| R ⁸ -S(=O) ₂ - | 33, 34 |
| R ⁸ -NH-C(=O)- | 30, 31, 54 |
| R⁸ | |
| C ₃₋₆ alkyl | 46 |
| C ₆₋₁₀ aryl | 17, 29, 30, 33, 49, 51, 53, 54 |
| C ₂₋₉ heteroaryl | 47, 48, 50, 52 |
| C ₆₋₁₀ aryl-C ₁₋₄ alkyl | 18, 21, 22, 25, 26, 27, 28, 31, 34 |
| C ₂₋₉ heteroaryl-C ₁₋₄ alkyl | 23, 24 |
| C ₃₋₁₀ cycloalkyl | 19 |
| C ₃₋₁₀ cycloalkyl-C ₁₋₄ alkyl | 20 |
| R¹ and R² | |
| C ₁₋₃ alkylene, which form a ring | 44, 45 |
| R² | |
| H | 1-15, 17-28, 30-35, 38-42 |
| C ₁₋₆ alkyl | 16, 29, 36, 37, 43 |
| R³ | |
| H | 1-54 |

Thus, Applicants have disclosed compounds , and in numerous cases, multiple compounds, with R moieties corresponding to those recited in the claims.

With regard to the Office's assertion that "[t]here is no reasonable basis for the assumption that the myriad of compounds embraced by the present formula (I) will share the same biological properties", Applicant's direct the Office's attention to page 31, lines 16-18 of the application at issue, wherein Applicants expressly stated that "[b]ased on the above testing protocols, we find that the compounds of the present invention and some of the intermediates used in the preparation thereof are active toward human δ receptors. In view of this statement, there is reason to believe the diversity among the substituent groups renders the claimed invention unenabled.

Applicants respectfully assert the specification of the present application enables one of ordinary skill in the art to use the claimed invention, as amended, without undue experimentation. In light of the direction provided by the 54 working examples, and the fact Applicants' specification discloses an example falling into nearly all of the presently claimed R^1 , R^2 , and R^3 moieties, Applicants' respectfully assert the full scope of the presently claimed invention is enabled. Accordingly, Applicants respectfully request the rejection of claims 1-10 and 18-23 under 35 U.S.C. §112, first paragraph, be withdrawn.

IV. Conclusion

Applicants respectfully submit the claims are in condition for allowance. An early notice of same is earnestly solicited. The Examiner is invited to contact Applicants' undersigned representative at (610) 640-7859 if there are any questions regarding Applicants' claimed invention.

The Commissioner is hereby authorized to debit any underpayment of fee due or credit any overpayment to Deposit Account No. 50-0436.

Respectfully submitted,

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